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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/171,697	10/23/98	TABAKOFF B	TBK-102-US

HM12/0827

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EXAMINER	
HUANG, E	
ART UNIT	**PAPER NUMBER**
1612	4

DATE MAILED: 08/27/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/171,697	Tabakoff
Examiner	**Group Art Unit**
Evelyn Huang	1612

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-23* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-23* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *2*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Claims 1-23 are pending.

2. Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 1, 10, 12, 21, the term 'suitable' is unclear since the criteria wherein it is 'suitable' have not been described in the specification; its deletion is recommended;

b. Claims 1, 12,

---the term 'general' in 'general formula I' is indefinite, its deletion is recommended;

---in the structural formula I, does applicant intend R2 and R3 to be attached to a nitrogen atom instead of the instant carbon atom? If so, it is unclear how R2 and R3 together with the intervening carbon atom represent carbonyl, thiocarbonyl etc.; clarification is required;

---it is unclear how Z can represent a group of formula=N, E; is E related to N?

c. Claims 10, 11, drawn to a composition, have no antecedent basis in the base claim 1, which is a method claim.

d. Claim 22, does applicant intend '5,7-dichloro' instead of the instant '5,7-dihydro'?

e. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board

stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1, 10, 12, 22 recite the broad recitation salt, and the claim also recite addition salt, which is the narrower statement of the range/limitation.

The rejection is applicable to the claims dependent on the above claims.

3. Applicant is advised that should claim 12 be found allowable, claim 20 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof because the compound is defined by its structures only, its inherent properties do not further limit the compound. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

4. Claims 1-9, 12, 21-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for using the compounds of claims 11, 23 for antagonizing NMDA receptor and inhibiting the voltage dependent sodium channel. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The following evaluation factors have been considered.

a. Nature of the invention. The instant invention is drawn to a N-substituted-4-ureido-2-carboxy quinoline compound, the method for treating withdrawal syndromes with the

inventive compound, and treating or preventing neuroexcitability disorders in a patient with an antagonist compound exhibiting affinity for both the strychnine-insensitive glycine binding site on NMDA receptor and voltage dependent sodium channels.

b. State the prior art and the level of the skill in the art. Compounds having diphenylureido group have been used to inhibit the voltage sensitive sodium channels (McNamara, cited by the applicant). Derivatives of kynurenic acid as antagonists of strychnine-insensitive glycine binding at the NMDA receptor have been described (Nichols I, 5493027; Harrison, 5606063).

The level of the skilled in the NMDA receptor antagonist art is high.

c. The predictability or unpredictability of the art. The high degree of unpredictability in the NMDA receptor antagonist art and the voltage dependent sodium channel inhibitor art is well known. A slight change in the structure of the compound would drastically change its biological activity as evidenced in the different degree of inhibition of glycine binding by structurally similar kynurenate derivatives (Nichols I, column 11, Table 8).

d. Amount of guidance/working examples. The preparation of the N,N-diphenyl-4-ureido-5, 7, -dichloro-2-carboxy-quinoline has been described. Compounds other than the 4-ureido-5, 7, -dihalo-2-carboxy-quinoline having affinity for both the strychnine-insensitive glycine binding site on NMDA receptor and voltage dependent sodium channels have not been described nor their method of making been disclosed. The procedures for assessing the binding for the strychnine-insensitive glycine binding site and the effects on sodium current and other NMDA-receptor mediated effects are described and the result shown for N,N-diphenyl-4-ureido-5, 7, -dichloro-2-carboxy-quinoline compounds in Figures 1-13.

e. Breadth of the claims. Applicant's assertion that all the structurally diverse compounds, including the undefined heterocycles, encompassed in the generic claims would have high affinity for both strychnine-insensitive glycine binding site on NMDA receptor and voltage dependent sodium channels does not commensurate with the scope of the objective enablement,

especially in view of the high degree of unpredictability and the working examples limited only to N,N-diphenyl-4-ureido-5, 7, -dichloro-2-carboxy-quinoline (paragraphs c-e above).

f. Quantitation of undue experimentation. Since insufficient guidance and teaching have been provided in the specification (paragraphs c-d above), one of ordinary skill in the art, even with high degree of skill, would not be able to make or use the invention as claimed without undue experimentation.

5. Nichols II (5783700) and Nichols III (5914403) discloses the instant 4-ureido-quinolic acid compounds (see claims). The patents have a filing date of 7-3-97, which is after the priority date of 6-6-97 of the instant application.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Evelyn Huang whose telephone number is (703) 305-7247.

EVELYN MEI HUANG
PRIMARY EXAMINER

August 20, 1999